

## IN THE CLAIMS

Please replace prior versions and listings of claims in the application with the following set of claims beginning on page 3 that follows.

New claims 51-88 amend the composition claims (1-37) of the original application, and claims 89-91 amend some of the previously presented method claims.

Claim 52 is the amended claim 2 of the original application and recites the several antimetabolites disclosed in the application with which the invention may be practiced. However, the Applicants had elected, with traverse, the antimetabolite of original claim 3 for examination in response to the restriction requirement of 7/29/05.

Hence, claim 52, which pertains to non-elected species has been indicated with the status identifier “withdrawn – new.”

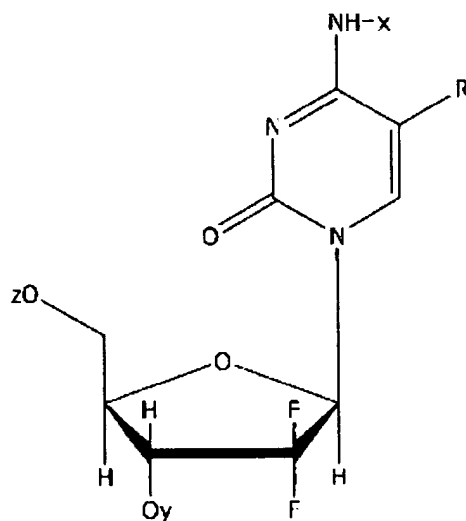
Claims 38-44 had previously been withdrawn, with traverse, in response to the restriction requirement.

No new matter has been introduced by this amendment.

## CLAIMS

1-37 (Canceled)

38. (Withdrawn) A compound having purity in excess of 98% by HPLC, having the formula:



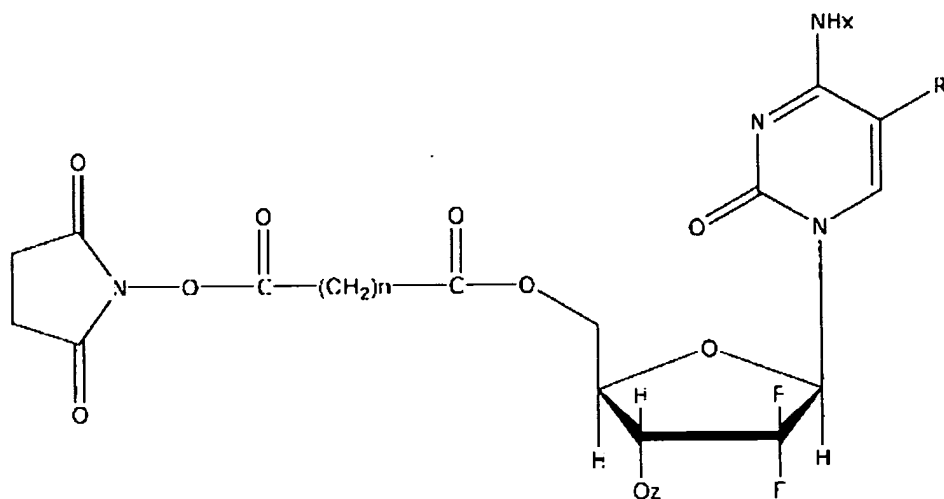
wherein R is selected from the group consisting of H, a C1-C6 alkyl, a halogen, a C2-C6 alkenyl, and a C2-C6 alkynyl;

x is an amine-protecting group that is stable in oligonucleotide synthesis conditions; and  
y, and z are each selected from H, a hydroxyl-protecting group that is stable in oligonucleotide synthesis conditions and a group that can be attached to a solid support.

39. (Withdrawn) The compound of claim 23, wherein the group that is attachable to a solid support has the formula  $O-C(=O)-M-C(=O)-NH\text{-Spacer}$ , where M is selected from the group consisting of succinyl, oxalyl, and hydroquinolynyl, and wherein the Spacer is selected from the

40. (Withdrawn) group consisting of a C1-C6 alkyl, ethoxyglycol, and a combination of alkyl and ethyleneglycoxy.

41. (Withdrawn) A compound having the formula:

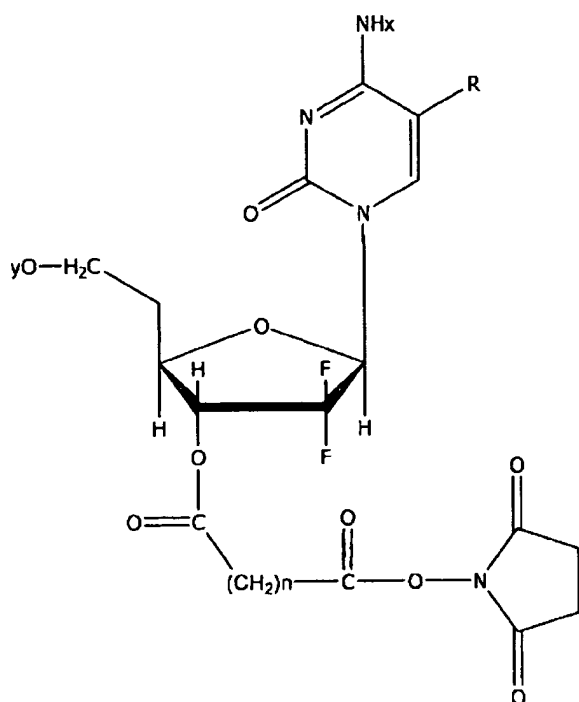


wherein R is selected from the group consisting of H, a C1-C6 alkyl, a halogen, a C2-C6 alkenyl, and a C2-C6 alkynyl;

x is an amine-protecting group that is stable in oligonucleotide synthesis conditions;

z is a hydroxyl-protecting group that is stable in oligonucleotide synthesis conditions; and  
n is 2-20.

42. (Withdrawn) A compound of the formula:



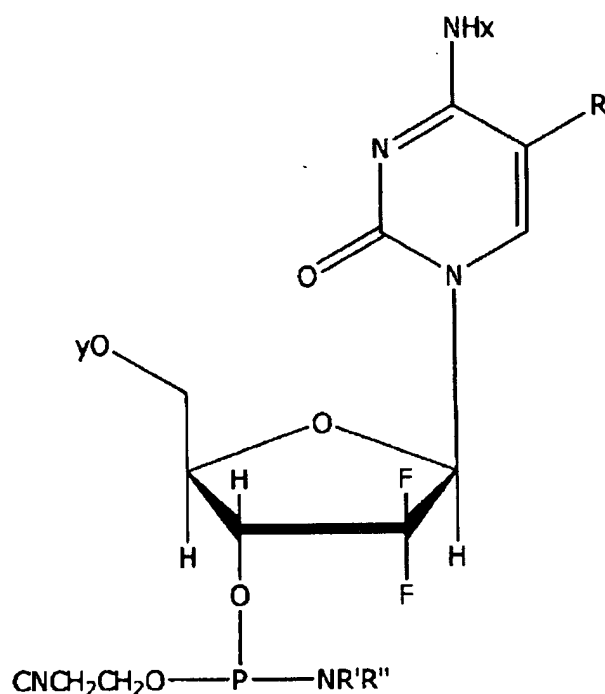
wherein R is selected from the group consisting of H, a C1-C6 alkyl, a halogen, a C2-C6 alkenyl, and a C2-C6 alkynyl;

x is an amine-protecting group that is stable in oligonucleotide synthesis conditions;

z is a hydroxyl-protecting group that is stable in oligonucleotide synthesis conditions; and

n is 2-20.

43. (Withdrawn) A compound having a purity in excess of 97% by HPLC, as shown by the formula:



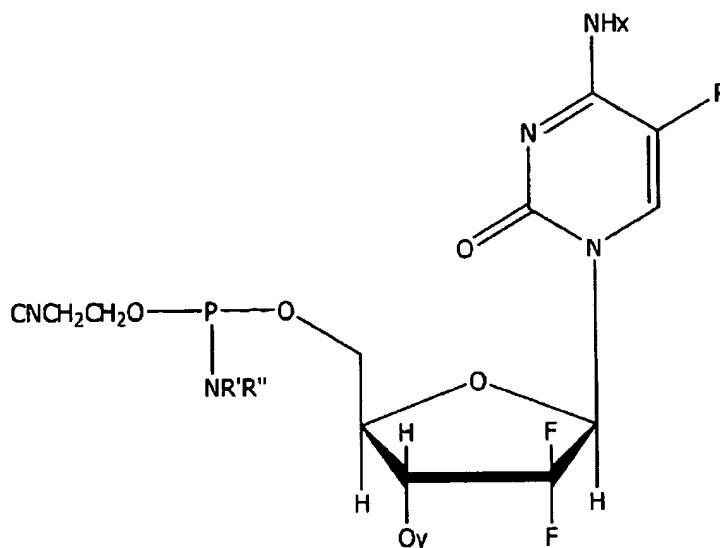
wherein y is a hydroxyl-protecting group that is stable in oligonucleotide synthesis conditions;

x is an amine-protecting group that is stable in oligonucleotide synthesis conditions;

R is selected from the group consisting of H, a C1-C6 alkyl, a halogen, a C2-C6 alkenyl, and a C2-C6 alkynyl; and

R' and R'' are independently selected from the group consisting of a C1-C6 alkyl and a C2-C6 cycloalkyl.

44. (Withdrawn) A compound having purity in excess of 97 % by HPLC, and having the formula:



wherein y is a hydroxyl-protecting group that is stable in oligonucleotide synthesis conditions;

x is an amine-protecting group that is stable in oligonucleotide synthesis conditions;

R is selected from the group consisting of H, a C1-C6 alkyl, a halogen, a C2-C6 alkenyl, and a C2-C6 alkynyl; and

R' and R'' are independently selected from the group consisting of a C1-C6 alkyl and a C2-C6 cycloalkyl.

45. – 50. (Canceled)

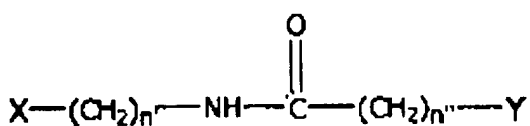
51. (New) An oligonucleotide for preferentially killing cancerous cells over noncancerous cells comprising at least two CpG moieties and a nucleoside antimetabolite covalently linked to the oligonucleotide.

52. (Withdrawn - new) The oligonucleotide of claim 51, wherein said nucleoside antimetabolite is selected from the group consisting of 2'-deoxy-3'-thiacytidine, 3'-azido-3'-deoxythymidine, 2',3'-dideoxycytidine, 2',3'-didehydro-3'-deoxythymidine, 2',3'-dideoxyinosine, 5-fluoro-2'-deoxy uridine, 2-fluoro-9-b-D-arabinofuranosyladenine, 1-B-D-arabinofuranosylcytosine, 5-azacytidine, 5-aza-2'-deoxycytidine, 6-mercaptopurineriboside, 2-chlorodeoxyadenosine, and pentostatin.
53. (New) The oligonucleotide of claim 51, wherein the nucleoside antimetabolite is 2'-deoxy, 2',2'-difluorocytidine.
54. (New) The oligonucleotide of claim 51, wherein two of said at least two CpG moieties are separated by a number of nucleotides selected from the numbers 2, 5, and 9.
55. (New) The oligonucleotide of claim 51, wherein said nucleoside antimetabolite is 5' to said at least two CpG moieties.
56. (New) The oligonucleotide of claim 51, wherein said nucleoside antimetabolite is 3' to said at least two CpG moieties.
57. (New) The oligonucleotide of claim 51, wherein said nucleoside antimetabolite is 3' to at least one CpG moiety and 5' to at least a second CpG moiety.
58. (New) The oligonucleotide of claim 51, wherein said nucleoside antimetabolite is linked to the oligonucleotide by a 3'-3' linkage.
59. (New) The oligonucleotide of claim 51, wherein said nucleoside antimetabolite is linked to the oligonucleotide by a 5'-5' linkage.
60. (New) The oligonucleotide of claim 51, wherein said nucleoside antimetabolite is linked to the oligonucleotide by a 3'-5' linkage.

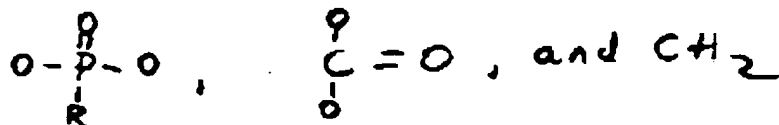
61. (New) The oligonucleotide of claim 51, wherein said nucleoside antimetabolite is covalently linked to the oligonucleotide by a 5'-3' linkage.

62. (New) The oligonucleotide of claim 51, wherein said nucleoside antimetabolite is at a position that is selected from 10 nucleotides upstream from one of the at least two CpG moieties, 9 nucleotides upstream from the CpG moiety, 8 nucleotides upstream from the CpG moiety, 7 nucleotides upstream from the CpG moiety, 6 nucleotides upstream from the CpG moiety, 5 nucleotides upstream from the CpG moiety, 4 nucleotides upstream from the CpG moiety, 3 nucleotides upstream from the CpG moiety, 2 nucleotides upstream from the CpG moiety, 1 nucleotides upstream from the CpG moiety, 10 nucleotides downstream from a CpG moiety, 9 nucleotides downstream from the CpG moiety, 8 nucleotides downstream from the CpG moiety, 7 nucleotides downstream from the CpG moiety, 6 nucleotides downstream from the CpG moiety, 5 nucleotides downstream from the CpG moiety, 4 nucleotides downstream from the CpG moiety, 3 nucleotides downstream from the CpG moiety, 2 nucleotides downstream from the CpG moiety, and 1 nucleotides downstream from the CpG moiety.

63. (New) The oligonucleotide of claim 1, wherein the nucleoside antimetabolite is covalently linked to the oligonucleotide by a linker having the formula.



wherein x and y are independently selected from



and R is selected from H, S, a C<sub>1</sub>-C<sub>6</sub> alkyl, a C<sub>1</sub>-C<sub>6</sub> alkoxy, and NH.

64. (New) The oligonucleotide of claim 51, wherein the oligonucleotide comprises at least one nucleotide having a ribose sugar moiety.
65. (New) The oligonucleotide of claim 51, wherein the oligonucleotide comprises at least one nucleotide having a 2'-deoxyribose sugar moiety.
66. (New) The oligonucleotide of claim 51, wherein the oligonucleotide comprises at least one 2'-halogen nucleotide.
67. (New) The oligonucleotide of claim 51, wherein the oligonucleotide comprises at least one 2'-N-alkyl nucleotide, wherein the alkyl has between about 1 and about 6 carbon atoms.
68. (New) The oligonucleotide of claim 51, wherein the oligonucleotide comprises at least one 2'-O-alkyl nucleotide, one 2'-N-Alkyl nucleotide, or one 2'-halogen nucleotide, wherein the alkyl has between about 1 and about 6 carbon atoms
69. (New) The oligonucleotide of claim 68, wherein the alkyl is methyl.
70. (New) The oligonucleotide of claim 51, wherein the oligonucleotide comprises a plurality of nucleotides connected by covalent internucleoside linkages, wherein each of the linkages are selected from the group consisting of a phosphodiester linkage, a C1-C6 alkoxy phosphotriester linkage, a phosphorothioate linkage and a phosphoramidate linkage.
71. (New) A pharmaceutical composition comprising the oligonucleotide of any of claims 51-70.
72. (New) A pharmaceutical composition of claim 71 further comprising a pharmaceutically acceptable carrier.
73. (New) The oligonucleotide of claim 72 wherein said pharmaceutically acceptable carrier is lipofectin.



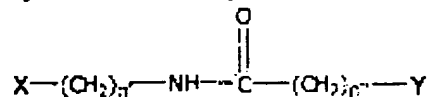
74. (New) An oligonucleotide for preferentially killing cancerous cells over noncancerous cells comprising a motif represented by one of the group of formulas 5'-PCGXCG-3' and 5'-CGXCGP-3', and wherein P is a nucleoside antimetabolite and X represents between 0 and 50 nucleotides.
75. (New) The oligonucleotide of claim 74, wherein the antimetabolite is 2'-deoxy, 2' -,2' -difluorocytidine.
76. (New) The oligonucleotide of claim of 74, where X is selected from the group consisting of 2, 5, and 9.
77. (New) The oligonucleotide of claim 74, wherein the oligonucleotide comprises multiple nucleotides and the nucleoside antimetabolite is covalently linked to one of the nucleotides by a 3'-3' linkage.
78. (New) The oligonucleotide of claim 74, wherein the oligonucleotide comprises multiple nucleotides and the nucleoside antimetabolite is covalently linked to one of the nucleotides by a 5'-5' linkage.
79. (New) The oligonucleotide of claim 74, wherein the oligonucleotide comprises multiple nucleotides and the nucleoside antimetabolite is covalently linked to one of the nucleotides by a 3'-5' linkage.
80. (New) The oligonucleotide of claim 74, wherein the oligonucleotide comprises 10 multiple nucleotides and the nucleoside antimetabolite is covalently linked to one of the nucleotides by a 5'-3' linkage.
81. (New) The oligonucleotide of claim 74, wherein the oligonucleotide comprises at least one nucleotide having a ribose sugar moiety.

82. (New) The oligonucleotide of claim 74, wherein the oligonucleotide comprises at least one nucleotide having a 2'-deoxyribose sugar moiety.

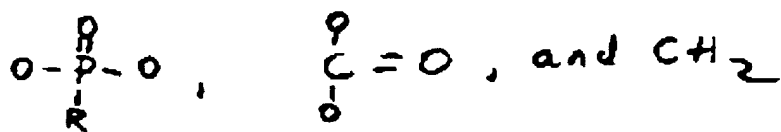
83. (New) The oligonucleotide of claim 74, wherein the oligonucleotide comprises at least one 2'-O-Alkyl nucleotide, 2'-N-Alkyl nucleotide, or 2'-halogen nucleotide, wherein the alkyl has between about 1 and about 6 carbon atoms.

84. (New) The oligonucleotide of claim 74, wherein the oligonucleotide comprises a plurality of nucleotides connected by covalent internucleoside linkages, wherein the linkages are selected from the group consisting of phosphodiester linkage, a C1-C6 alkoxy phosphotriester linkage, a phosphorothioate linkage and a phosphoramidate linkage.

85. (New) The oligonucleotide of claim 74, wherein the oligonucleotide comprises 30 multiple nucleotides and the nucleoside antimetabolite is attached to at least one of the multiple nucleotides by a linker having the formula.



wherein x and y are independently selected from



and R is selected from H, S, a C1-C6 alkyl, a C1-C6 alkoxy, and NH.

86. (New) A pharmaceutical composition comprising the oligonucleotide of any of claims 74-85.

87. (New) A pharmaceutical composition of claim 74 further comprising a pharmaceutically acceptable carrier.

88. (New) The oligonucleotide of claim 86 wherein said pharmaceutically acceptable carrier is lipofectin.

89. (New) The method of synthesizing an oligonucleotide product for preferentially killing cancerous cells over non- cancerous cells comprising the steps of:

- (a) Selecting an oligonucleotide comprising at least two CpG moieties; and
- (b) Covalently linking a nucleoside antimetabolite to said oligonucleotide comprising at least two CpG moieties.

90. (New) The method of claim 89, wherein said oligonucleotide comprising at least two CpG moieties comprises between 2 and 50 nucleotides.

91. (New) The method of claim 89, wherein said nucleoside antimetabolite is 2'-deoxy, 2',2'-difluorocytidine.